

# Expression of SARS-CoV-2 entry receptors in human skin and their upregulation during inflammation suggest a potential risk for cutaneous transmission

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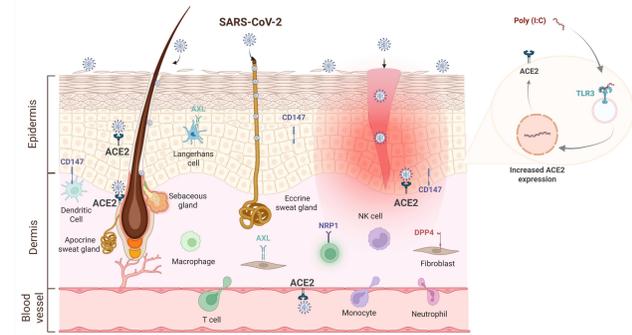


## HIGHLIGHTS

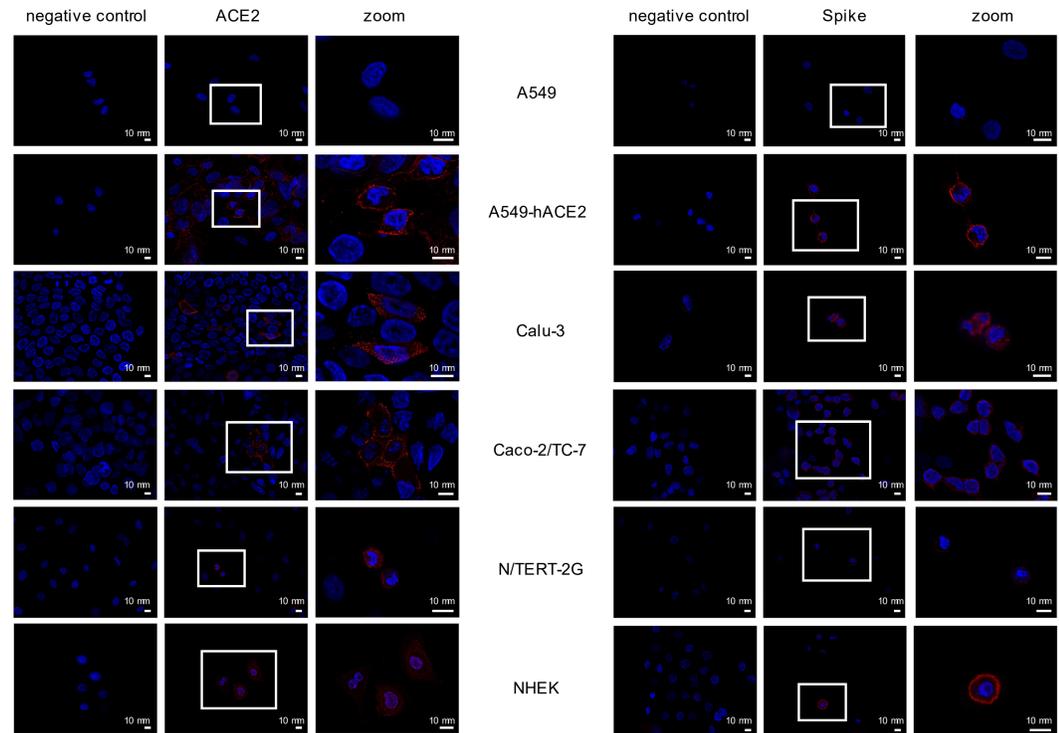
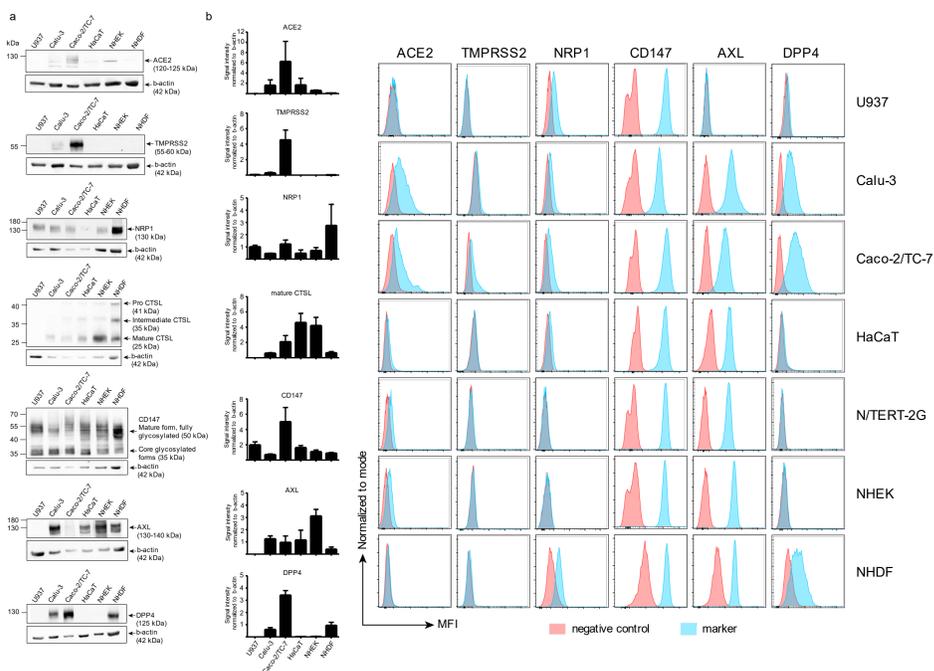
**AIM:** to investigate further the mechanisms by which SARS-CoV-2 may enter the skin and whether local replication occurs

### RESULTS:

- SARS-CoV-2 entry receptors except TMPRSS2 are expressed in human skin
- Binding of Spike to ACE2 and expression of mature CTSL in primary keratinocytes suggests that viral entry may occur via endocytosis
- TLR3-mediated increase of ACE2 expression may facilitate SARS-CoV-2 infection
- In vitro infection with SARS-CoV-2 show that the virus can bind and enter keratinocytes but cannot replicate within the cells, suggesting a restriction at entry or early after infection.



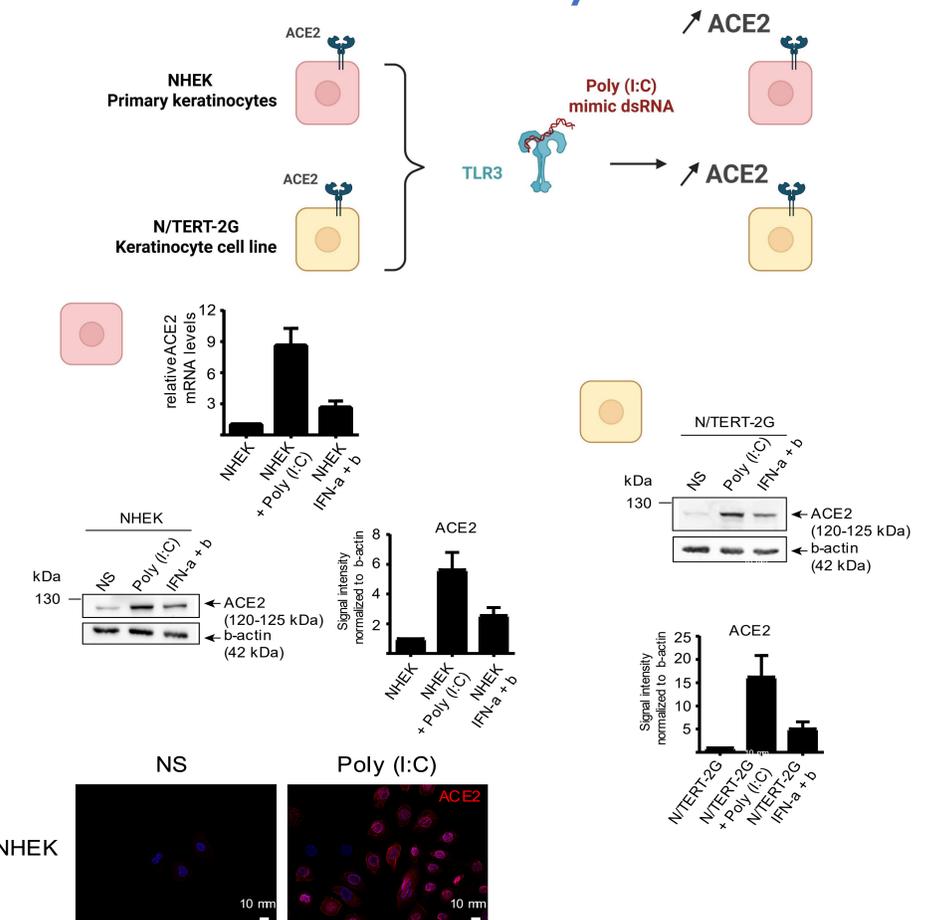
## Expression of SARS-CoV-2 receptors and SPIKE binding in healthy skin



➤ All tested SARS-CoV-2 entry receptors, co-receptors and proteases, except TMPRSS2, are expressed in human skin

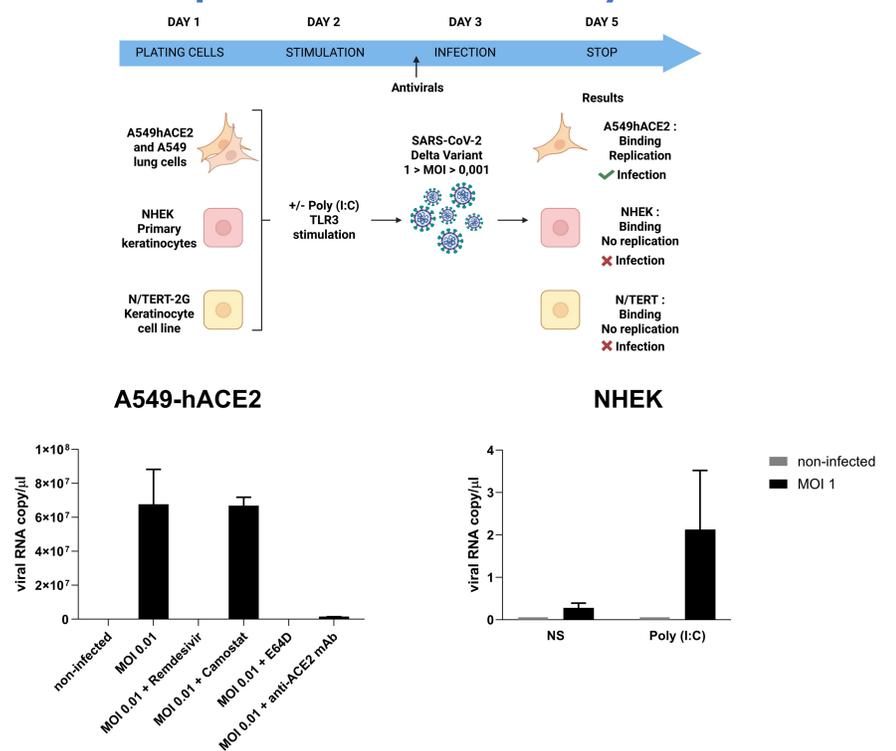
➤ Expression of ACE2, mature CTSL and the binding of Spike to primary keratinocytes suggests SARS-CoV-2 could enter via endocytosis

## TLR3-mediated activation upregulates ACE2 expression in human epidermal keratinocytes



➤ Skin inflammation, through TLR3 activation and type I interferon signaling promotes ACE2 expression in keratinocytes, potentially enhancing their susceptibility to SARS-CoV-2 infection

## In vitro SARS-CoV-2 infection of human epidermal keratinocytes



➤ The virus can bind to primary keratinocytes but does not replicate

## Conclusion

Although active viral replication in keratinocytes is unlikely, the presence and inducible upregulation of ACE2 in response to inflammatory stimuli may confer a limited potential for cutaneous viral entry, warranting further investigation into the role of skin in SARS-CoV-2 transmission